**AMENDMENTS**



**IN THE CLAIMS:**

Kindly amend the claims as follows:

Please cancel claims 1-4.

Please add new claim 9:

9. (New) An hIL-4 mutein having a reduced affinity and/or an altered specificity to the γ subunit of the IL-4 receptor and/or HIL-13 R α subunit of the hIL-4 receptor, wherein one or more amino acids at positions 7, 11, 12, 15, 121, 123, 124, or 125 have been substituted with another amino acid.

## REMARKS

Applicants respectfully request reconsideration and reexamination of the present application in light of the amendments and the remarks below.

An abstract has been provided on a separate sheet.

Claims 1-8 are pending in this application. Claims 1-4 have been cancelled, and claims 5-8 have been withdrawn from consideration as being drawn to a nonelected invention, as recited in page 1 of Paper No. 10. New claim 9 has been added.

By these amendments, the Applicants do not acquiesce to the propriety of any of the Examiner's rejections and in particular, Applicants retain their rights to file divisional and/or continuation applications directed to any cancelled subject matter. These amendments are made to clarify the subject matter therein, as discussed below. These amendments, therefore, do not disclaim any subject matter to which the Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997); *and Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 56 U.S.P.Q.2d 1865 (Fed. Cir. 2000).

As amended, the invention relates to hIL-4 muteins, wherein one or more amino acids at positions 7, 11, 12, 15, 121, 123, 124, or 125 are substituted with another amino acid. Support for the new claim may be found in the specification, for example, at page 7, line 11-line 22. In particular, the present invention demonstrates that amino acid substitutions at positions 7, 11, 12, 15, 121, 123, 124, or 125 of hIL-4 yield hIL-4 muteins which bind to the γ chain of the IL-4 receptor with reduced affinity (*see, e.g.,* Table 1 and 2 at pages 21 and 22). That is, as compared to the dissociation constant ($K_d$) of IL-4, the $K_d$ values of the claimed hIL-4 muteins are greater, indicating a reduced affinity for the γ chain. Variants with substitutions at other amino acid positions exhibited dissociation rate constants similar to wild type IL-4, thus demonstrating that amino acids at positions 7, 11, 12, 15, 121, 123, 124, or 125 are critical for γ chain binding (*see, e.g.,* Table 1 and 2 at pages 21 and 22). Furthermore, large hydrophobic residue substitutions do not lead to a loss in γ chain binding, and thus may account for altered specificity (*see, e.g.,* page 10, line 31-page 11, line 13). Therefore, the specification does provide guidance to produce an hIL-4 mutein with reduced affinity or altered specificity.

With respect to Wang et al., 1997 and Kruse et al., 1993, neither Wang et al., nor Kruse et al., teach or suggest the combination of amino acid substitutions at positions 7, 11, 12, 15, 121, 123, 124, or 125 of the hIL-4 muteins of the present invention. Furthermore, neither Wang et al., nor Kruse et al., teach or suggest that amino acids at positions 7, 11, 12, 15, 121, 123, 124, or 125 are critical for γ chain binding or specificity. Thus, Wang et al., and Kruse et al., do not teach each and every limitation of the claimed invention.

## CONCLUSION

For the foregoing reasons, Applicants submit that the claim is in condition for allowance and Applicants respectfully request reexamination of the present application, reconsideration and withdrawal of the present rejections and entry of the amendments. Should there be any further matter requiring consideration, Examiner Seharaseyon is invited to contact the undersigned counsel.

If there are any further fees due in connection with the filing of the present reply, please charge the fees to undersigned's Deposit Account No. 13-3372. If a fee is required for an extension of time not accounted for, such an extension is requested and the fee should also be charged to undersigned's deposit account.

Respectfully submitted,

February 22, 2002

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